15	101	"large DNA fragments" and (escherichia and streptomyces)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
20	207	((streptomyces and rapamycin) and ("binary vector" or "shuttle vector")) and ("100 kb" or "150 kb" or "300 kb")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
19	127	(vector) SAME (attb or attp)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
23	391	(actinomycete or actinomycetales) and (rapamycin or erythromycin or rifamycin)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
21	29	(((streptomyces and rapamycin) and ("binary vector" or "shuttle vector")) and ("100 kb" or "150 kb" or "300 kb")) and "e.coli"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
25	207	(((actinomycete or actinomycetales) and (rapamycin or erythromycin or rifamycin)) and ("shuttle vector" or "binary vector")) and ("100" kb or 100kb or 150kb or "150" kb or "300" kb or 300kb)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
22	22	actinomycete SAME ("DNA fragment" or "genomic DNA")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
24	207	((actinomycete or actinomycetales) and (rapamycin or erythromycin or rifamycin)) and ("shuttle vector" or "binary vector")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
26	11	("binary vector" or "shuttle vector") SAME (attb or attp)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
28	2470	"100 kb" or "100kb" or "150kb" or "150 kb" or "300 kb" or "300kb"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:29
27	10	"stable maintenance" SAME "large DNA"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:28
29	42160	((435/6|435/91.1|435/172.1|435/252.35|435/320.1).ccls.)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:30
30	3	(((435/6|435/91.1|435/172.1|435/252.35|435/320.1).ccls.)) and actinomyce	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 17:30

L Number	Hits	Search Text	DB	Time stamp
1	101	"large DNA fragments" and (escherichia and streptomyces)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:41
2	8	"large DNA fragments" and (escherichia and streptomycete)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:41
3	127	(vector) SAME (attb or attp)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:41
4	207	((actinomycete or actinomycetales) and (rapamycin or erythromycin or rifamycin)) and ("shuttle vector" or "binary vector")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:41
5	1124	streptomyces and rapamycin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:41
6	11	("binary vector" or "shuttle vector") SAME (attb or attp)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:41
7	277	(streptomyces and rapamycin) and ("binary vector" or "shuttle vector")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:42
8	10	"stable maintenance" SAME "large DNA"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:42
10	2470	"100 kb" or "100kb" or "150kb" or "150 kb" or "300 kb" or "300kb"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:42
11	207	((streptomyces and rapamycin) and ("binary vector" or "shuttle vector")) and ("100 kb" or "150 kb" or "300 kb")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:42
12	29	(((streptomyces and rapamycin) and ("binary vector" or "shuttle vector")) and ("100 kb" or "150 kb" or "300 kb")) and "e.coli"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:42
15	207	(((actinomycete or actinomycetales) and (rapamycin or erythromycin or rifamycin)) and ("shuttle vector" or "binary vector")) and ("100" kb or 100kb or 150kb or "150" kb or "300" kb or 300kb)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:42
16	22	actinomycete SAME ("DNA fragment" or "genomic DNA")	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:42
18	2278	actinomycete or actinomycetales	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:43
19	391	(actinomycete or actinomycetales) and (rapamycin or erythromycin or rifamycin)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:43
20	2	4921801.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:43
21	2	5866410.pn.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:43

22	0	(((streptomyces and rapamycin) and ("binary vector" or "shuttle vector")) and ("100 kb" or "150 kb" or "300 kb")) and "e. coli"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:43
23	0	((vector) SAME (attb or attp)) and (actinomycet or streptomycet)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:43
24	0	"interplasmid homologous recombination"	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:43
25	0	"large DNA fragments" SAME (escherichia and streptomyce)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/01/20 18:44

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 FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 18:24:51 ON 20 JAN 2004
L1       168696 S ACTINOMYCE?
L2          268 S L1 AND ("SHUTTLE VECTOR" OR "BINARY VECTOR" OR "BIFUNCTIONAL
L3          247 DUP REM L2 (21 DUPLICATES REMOVED)
L4          199 S L3 NOT PY>=2000
L5            0 S L4 AND (ATTB OR ATTP)
L6            0 S L4 AND (INT-TSR OR TSR-INT)
L7            0 S L4 AND "INTERPLASMID"
L8           63 S STREPTOMYCES AND "SITE SPECIFIC RECOMBINATION"
L9           27 DUP REM L8 (36 DUPLICATES REMOVED)
L10          19 S L9 NOT PY>=2000
L11       47105 S STREPTOMYCES
L12         140 S L11 AND (ATTP OR ATTB OR INT-TSR)
L13          53 DUP REM L12 (87 DUPLICATES REMOVED)
L14          36 S L13 NOT PY>=2000
L15        1093 S L11 AND (RAPAMYCIN OR ERYTHROMYCIN OR RIFAMYCIN)
L16          46 S L15 AND (E.COLI OR "E. COLI" OR "E.COLI")
L17          27 DUP REM L16 (19 DUPLICATES REMOVED)
L18          16 S L17 NOT PY>=2000
L19          50 S L11 AND ("100KB" OR "100 KB" OR "150KB" OR "150 KB" OR "300 K
L20          20 DUP REM L19 (30 DUPLICATES REMOVED)
L21          11 S L20 NOT PY>=2000
L22          10 S L11 AND "STABLE MAINTENANCE"
L23           5 DUP REM L22 (5 DUPLICATES REMOVED)
L24          42 S "INTERPLASMID RECOMBINATION"
L25          17 DUP REM L24 (25 DUPLICATES REMOVED)
L26          14 S L25 NOT PY>=2000
L27       22638 S L1 AND L11
L28          32 S L27 AND "SITE SPECIFIC RECOMBINATION"
L29          25 DUP REM L28 (7 DUPLICATES REMOVED)
L30          18 S L29 NOT PY>=2000
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21 ANSWER 1 OF 11 MEDLINE on STN
ACCESSION NUMBER: 1998332731 MEDLINE
DOCUMENT NUMBER: 98332731 PubMed ID: 9666116
TITLE: amlC, another amylolytic gene maps close to the amlB locus in **Streptomyces** lividans TK24.
AUTHOR: Yin X H; Gerbaud C; Francou F X; Guerineau M; Virolle M J
CORPORATE SOURCE: Laboratoire de Biologie et Genetique Moleculaire, Institut de Genetique et Microbiologie, CNRS URA D2225 Batiment 400, Universite Paris-Sud, F-91405, Orsay, Cedex, France.
SOURCE: GENE, (1998 Jul 17) 215 (1) 171-80.
Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-Z86113
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980904

AB The region located upstream of the alpha-amylase gene (amlB) of **Streptomyces** lividans TK24 (Yin et al., 1997) contains a 2978-bp-long ORF divergent from amlB, and designated amlC. amlC Encodes a 993amino acid (aa) protein with a calculated molecular weight of 107.054kDa. On the basis of sequence similarity as well as enzymatic activity, AmlC is likely to belong to the 1, 4-alpha-D-glucan glucanohydrolase family. amlC is transcribed as a unique 3kb leaderless monocistronic mRNA. Primer extension experiments allowed the identification of promoter sequences that do not resemble the typical eubacterial promoter sequences. amlC was successfully disrupted and was mapped at approx. 700kb from a chromosomal end of S. lividans TK24, **100kb** on the right of the amplifiable unit AUD1 (Volff et al., 1996). Nevertheless, amlC disruption seemed to be accompanied by extensive rearrangements of the 2500-kb DraI-II fragment of the chromosome.

L21 ANSWER 2 OF 11 MEDLINE on STN
ACCESSION NUMBER: 1998083067 MEDLINE
DOCUMENT NUMBER: 98083067 PubMed ID: 9422604
TITLE: Molecular cloning and physical mapping of the daptomycin gene cluster from **Streptomyces** roseosporus.
AUTHOR: Mchenney M A; Hosted T J; Dehoff B S; Rosteck P R Jr; Baltz R H
CORPORATE SOURCE: Lilly Research Laboratories, A Division of Eli Lilly and Company, Indianapolis, Indiana 46285, USA.
SOURCE: JOURNAL OF BACTERIOLOGY, (1998 Jan) 180 (1) 143-51.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF021262; GENBANK-AF021263
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 20030325
Entered Medline: 19980203

AB The daptomycin biosynthetic gene cluster of **Streptomyces** roseosporus was analyzed by Tn5099 mutagenesis, molecular cloning, partial DNA sequencing, and insertional mutagenesis with cloned segments of DNA. The daptomycin biosynthetic gene cluster spans at least 50 kb and is located about 400 to 500 kb from one end of the approximately 7, **100-kb** linear chromosome. We identified two peptide synthetase coding regions interrupted by a 10- to 20-kb region that may

encode other functions in lipopeptide biosynthesis.

L21 ANSWER 3 OF 11 MEDLINE on STN
ACCESSION NUMBER: 97188523 MEDLINE
DOCUMENT NUMBER: 97188523 PubMed ID: 9037108
TITLE: Chromosomal deletions in **Streptomyces** griseus that remove the afsA locus.
AUTHOR: Lezhava A; Kameoka D; Sugino H; Goshi K; Shinkawa H; Nimi O; Horinouchi S; Beppu T; Kinashi H
CORPORATE SOURCE: Department of Fermentation Technology, Hiroshima University, Higashi-Hiroshima, Japan.
SOURCE: MOLECULAR AND GENERAL GENETICS, (1997 Jan 27) 253 (4) 478-83.
Journal code: 0125036. ISSN: 0026-8925.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970312

AB We have recently constructed a physical map of the **Streptomyces** griseus 2247 genome using the restriction enzymes AseI and DraI, which revealed that this strain carries a 7.8 Mb linear chromosome. Based on this map, precise macrorestriction fragment and cosmid maps were constructed for both ends of the chromosome, which localized the afsA gene **150 Kb** from the left end. Two afsA- mutants were found to have suffered chromosomal deletions that removed the afsA locus. The sizes of the deletions were 20 and 130 Kb at the right end and 180 and 350 kb at the left end, respectively. Hybridization experiments using cosmids carrying a deletion endpoint indicated that the ends of the chromosome in the mutants were fused to form a circular chromosome.

L21 ANSWER 4 OF 11 MEDLINE on STN
ACCESSION NUMBER: 95146425 MEDLINE
DOCUMENT NUMBER: 95146425 PubMed ID: 7844039
TITLE: Isolation and characterization of linear plasmids from lankacidin-producing **Streptomyces** species.
AUTHOR: Kinashi H; Mori E; Hatani A; Nimi O
CORPORATE SOURCE: Department of Fermentation Technology, Faculty of Engineering, Hiroshima University, Japan.
SOURCE: JOURNAL OF ANTIBIOTICS, (1994 Dec) 47 (12) 1447-55.
Journal code: 0151115. ISSN: 0021-8820.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950316
Last Updated on STN: 19950316
Entered Medline: 19950306

AB **Streptomyces** rochei 7434AN4, a producer of lankacidin and lankamycin contains three large linear plasmids, pSLA2-L (200 kb), M (**100 kb**), and S (17 kb). Studies on the mutants of 7434AN4 having a different plasmid profile showed a parallel relationship between the presence of pSLA2-L and the production of both lankacidin and lankamycin. When pSLA2-L was transferred by protoplast fusion to S. rochei 2-39, a non-antibiotic-producing mutant of 7434AN4 which contained no detectable plasmid, the fusants gained the capacity to produce both antibiotics. From the physical maps of pSLA2-L and pSLA2-L1, a deletion plasmid (160 kb) of pSLA2-L, the latter plasmid was determined to contain a symmetrical linear repeat composed of the right 80-kb part of pSLA2-L.

Four other lankacidin-producing **Streptomyces** strains were also found to have distinctive large linear plasmids which hybridized with the pSLA2-L probe. These results support the involvement of pSLA2-L in the production of lankacidin and lankamycin in S. rochei 7434AN4.

L21 ANSWER 5 OF 11 MEDLINE on STN
ACCESSION NUMBER: 95124297 MEDLINE
DOCUMENT NUMBER: 95124297 PubMed ID: 7823911
TITLE: DNA amplifications and deletions in **Streptomyces** lividans 66 and the loss of one end of the linear chromosome.
AUTHOR: Rauland U; Glocker I; Redenbach M; Cullum J
CORPORATE SOURCE: Universitat Kaiserslautern, Germany.
SOURCE: MOLECULAR AND GENERAL GENETICS, (1995 Jan 6) 246 (1) 37-44. Journal code: 0125036. ISSN: 0026-8925.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19950223
Entered Medline: 19950215

AB Thirty-two 2-deoxygalactose-resistant mutants with DNA amplifications were isolated from **Streptomyces** lividans 66 strains carrying plasmid pMT664, which carries an agarase gene (dagA) and IS466. Thirty-one of the mutants carried amplified DNA sequences from a 70 kb region about **300 kb** from one end of the linear chromosome in this species. In 28 of the mutants, all the wild-type sequences between the amplified region and the start of the 30 kb inverted repeat that forms the chromosome end were deleted. Thus, there appeared to be loss of one chromosome end and its replacement by the DNA amplification. In some mutants there amplification of a previously characterised 5.7 kb sequence that lies about 600 kb from the other chromosome end was also noted.

L21 ANSWER 6 OF 11 MEDLINE on STN
ACCESSION NUMBER: 94362904 MEDLINE
DOCUMENT NUMBER: 94362904 PubMed ID: 8081502
TITLE: Characterization of a **Streptomyces**-lividans-type site-specific DNA modification system in the avermectin-producer **Streptomyces** avermitilis permits investigation of two novel giant linear plasmids, pSA1 and pSA2.
AUTHOR: Evans M; Kaczmarek F S; Stutzman-Engwall K; Dyson P
CORPORATE SOURCE: Molecular Biology Research Group, School of Biological Sciences, University College of Swansea, Singleton Park, UK.
SOURCE: MICROBIOLOGY, (1994 Jun) 140 (Pt 6) 1367-71. Journal code: 9430468. ISSN: 1350-0872.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 19941021
Last Updated on STN: 19941021
Entered Medline: 19941010

AB The degradation of **Streptomyces** avermitilis DNA samples analysed by conventional pulsed-field gel electrophoresis was shown to be due to Tris-dependent, double-strand cleavage. Using alternative electrophoretic conditions, separation of intact DNA molecules was achieved, permitting the identification of two novel giant linear plasmids: the **100 kb** pSA1 and 250 kb pSA2. Use of pSA2 DNA as a probe showed that

pSA1 does not cross-hybridize, indicating that the plasmids are not closely related. The site-specificity of the DNA modifications, which render the DNA susceptible to Tris-dependent cleavage, was found to be essentially identical to that of similar modifications found in the DNA of S. lividans.

L21 ANSWER 7 OF 11 MEDLINE on STN
ACCESSION NUMBER: 93239680 MEDLINE
DOCUMENT NUMBER: 93239680 PubMed ID: 8478321
TITLE: Deletion analysis of the avermectin biosynthetic genes of **Streptomyces** avermitilis by gene cluster displacement.
AUTHOR: MacNeil T; Gewain K M; MacNeil D J
CORPORATE SOURCE: Department of Microbial Chemotherapeutics and Molecular Genetics, Merck Research Laboratories, Rahway, New Jersey 07065.
SOURCE: JOURNAL OF BACTERIOLOGY, (1993 May) 175 (9) 2552-63. Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930611
Last Updated on STN: 19970203
Entered Medline: 19930526

AB **Streptomyces** avermitilis produces a group of glycosylated, methylated macrocyclic lactones, the avermectins, which have potent anthelmintic activity. A homologous recombination strategy termed gene cluster displacement was used to construct Neor deletion strains with defined endpoints and to clone the corresponding complementary DNA encoding functions for avermectin biosynthesis (avr). Thirty-five unique deletions of 0.5 to > **100 kb** over a continuous **150-kb** region were introduced into S. avermitilis. Analysis of the avermectin phenotypes of the deletion-containing strains defined the extent and ends of the 95-kb avr gene cluster, identified a regulatory region, and mapped several avr functions. A 60-kb region in the central portion determines the synthesis of the macrolide ring. A 13-kb region at one end of the cluster is responsible for synthesis and attachment of oleandrose disaccharide. A 10-kb region at the other end has functions for positive regulation and C-5 O methylation. Physical analysis of the deletions and of in vivo-cloned fragments refined a 130-kb physical map of the avr gene cluster region.

L21 ANSWER 8 OF 11 MEDLINE on STN
ACCESSION NUMBER: 92331948 MEDLINE
DOCUMENT NUMBER: 92331948 PubMed ID: 1628843
TITLE: Plasmid cloning vectors for the conjugal transfer of DNA from Escherichia coli to **Streptomyces** spp.
AUTHOR: Bierman M; Logan R; O'Brien K; Seno E T; Rao R N; Schoner B E
CORPORATE SOURCE: Lilly Research Laboratories, A Division of Eli Lilly and Company, Indianapolis, IN 46285-0424.
SOURCE: GENE, (1992 Jul 1) 116 (1) 43-9. Journal code: 7706761. ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920904
Last Updated on STN: 19920904
Entered Medline: 19920817

AB We have constructed cloning vectors for the conjugal transfer of DNA from Escherichia coli to **Streptomyces** spp. All vectors contain the 760-bp oriT fragment from the IncP plasmid, RK2. Transfer functions need to be supplied in trans by the E. coli donor strain. We have incorporated into these vectors selectable antibiotic-resistance markers (AmR, ThR, SpR) that function in **Streptomyces** spp. and other features that should allow for: (i) integration via homologous recombination between cloned DNA and the **Streptomyces** spp. chromosome, (ii) autonomous replication, or (iii) site-specific integration at the bacteriophage phi C31 attachment site. Shuttle cosmids for constructing genomic libraries and bacteriophage P1 cloning vector capable of accepting approx. **100-kb** fragments are also described. A simple mating procedure has been developed for the conjugal transfer of these vectors from E. coli to **Streptomyces** spp. that involves plating of the donor strain and either germinated spores or mycelial fragments of the recipient strain. We have shown that several of these vectors can be introduced into **Streptomyces** fradiae, a strain that is notoriously difficult to transform by PEG-mediated protoplast transformation.

L21 ANSWER 9 OF 11 MEDLINE on STN
ACCESSION NUMBER: 89364731 MEDLINE
DOCUMENT NUMBER: 89364731 PubMed ID: 2770699
TITLE: Extremely large chromosomal deletions are intimately involved in genetic instability and genomic rearrangements in **Streptomyces** glaucescens.
AUTHOR: Birch A; Hausler A; Vogtli M; Krek W; Hutter R
CORPORATE SOURCE: Mikrobiologisches Institut, Eidgenossische Technische Hochschule, Zurich, Switzerland.
SOURCE: MOLECULAR AND GENERAL GENETICS, (1989 Jun) 217 (2-3) 447-58.
Journal code: 0125036. ISSN: 0026-8925.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891012

AB Genetic instability in **Streptomyces** glaucescens characteristically involves the occurrence of gross genomic rearrangements including high-level sequence amplification and extensive deletion. We investigated the relationship of the unstable melC and strS loci and a **100 kb** region of the chromosome which frequently gives rise to intense heterogeneous DNA amplification. Standard chromosome walking using a cosmid bank in conjunction with a "reverse-blot" procedure enabled us to construct a contiguous genomic BamHI map of the unstable region exceeding 900 kb. The unstable genes and the amplifiable region (AUD locus) are physically linked within a 600 kb segment of the chromosome. The previously characterized deletions which affect these loci are merely components of much larger deletions ranging from 270 to over 800 kb which are polar in nature, effecting the sequential loss of the strS and melC loci. The more extensive deletions terminate either adjacent to, or in the vicinity of DNA reiterations at the AUD locus. Additionally, a deletion junction fragment and the corresponding deletion ends were cloned and analysed at the sequence level.

L21 ANSWER 10 OF 11 MEDLINE on STN
ACCESSION NUMBER: 89364730 MEDLINE
DOCUMENT NUMBER: 89364730 PubMed ID: 2770698
TITLE: Heterogeneous genomic amplification in **Streptomyces** glaucescens: structure, location and junction sequence

analysis.

AUTHOR: Hausler A; Birch A; Krek W; Piret J; Hutter R
CORPORATE SOURCE: Mikrobiologisches Institut, Eidgenossische Technische Hochschule, Zurich, Switzerland.
SOURCE: MOLECULAR AND GENERAL GENETICS, (1989 Jun) 217 (2-3) 437-46.
Journal code: 0125036. ISSN: 0026-8925.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19970203
Entered Medline: 19891012

AB Certain chromosomal markers in **Streptomyces** glaucescens behave unstably, being lost at high frequency as a result of extensive genomic deletion. Additionally, mutant strains possessing such deletions frequently display intense DNA amplification. With the help of a wild-type cosmid library we investigated the structure of the amplified DNA sequences (ADS) and the corresponding wild-type amplifiable units of DNA (AUD). The reiterations were heterogeneous in location, copy number and sequences involved and originated predominantly from a single **100 kb** region of the chromosome called the AUD locus.
All strains bearing reiterations possessed associated deletions which terminated either close to or at the ADS. The termini of four AUDs were sequenced in order to gain more knowledge about these heterogeneous amplifications. In three of the four cases investigated small, interrupted homologies were found bordering the AUDs. With the help of orthogonal-field-alternation gel electrophoresis (OFAGE) we were able to visualize a tandem reiteration of more than 1,500 kb in length.

L21 ANSWER 11 OF 11 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:106824 BIOSIS
DOCUMENT NUMBER: PREV199698678959
TITLE: Genetic instability in **Streptomyces** lividans 66.
AUTHOR(S): Cullum, John [Reprint author]; Redenbach, Matthias; Arnold, Annette; Rauland, Uwe [Reprint author]; Sutter, Hans [Reprint author]
CORPORATE SOURCE: LB Genet., Univ. Kaiserslautern, Postfach 3049, D-67653 Kaiserslautern, Germany
SOURCE: Biotekhnologiya, (1995) Vol. 0, No. 7-8, pp. 95-98.
CODEN: BTKNEZ. ISSN: 0234-2758.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Mar 1996
Last Updated on STN: 12 Mar 1996

AB Two amplifiable regions (AUD) of the S. lividans 66 chromosome were studied. AUD-5.7 gives rise to reproducible 5.7 kb amplifications and lies about 600 kb away from the linear chromosome end. AUD-Type1 gives rise to a variety of amplifications with differing end points within the 70 kb region, which lies about **300 kb** from the other chromosome end. In most of the latter amplifications all sequences between the amplification and the chromosome end were deleted. It appeared that the closer chromosome end had been deleted, but that the other end was intact. A variety of deletions involving the chromosome ends were isolated. However, no strains were found in which only the chromosome end closer to AUD-5.7 had been deleted. Deletions affecting this end of the chromosome seemed to always result in loss of both ends and a hot spot for deletion was found. The significance of these data for models of genetic instability will be discussed.

ACCESSION NUMBER: 88198008 MEDLINE
DOCUMENT NUMBER: 88198008 PubMed ID: 2834330
TITLE: Site-specific insertion of biologically functional adventitious genes into the **Streptomyces** lividans chromosome.
AUTHOR: Omer C A; Stein D; Cohen S N
CORPORATE SOURCE: Department of Genetics, Stanford University School of Medicine, California 94305.
CONTRACT NUMBER: GM07790 (NIGMS)
GM26355 (NIGMS)
SOURCE: JOURNAL OF BACTERIOLOGY, (1988 May) 170 (5) 2174-84.
Journal code: 2985120R. ISSN: 0021-9193.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198806
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19990129
Entered Medline: 19880609

AB We report that transformation of **Streptomyces** lividans with cloned DNA of the SLP1 genetic element results in integration of the element at the same chromosomal locus (attB) normally occupied by SLP1 in its original host, **Streptomyces** coelicolor, and in S. lividans that has received SLP1 by mating. We constructed SLP1 derivatives that can integrate foreign DNA at the attB site and used these to introduce adventitious DNA sequences into the S. lividans chromosome. We also identified three regions of SLP1 essential for its integration and demonstrated that integration of the SLP1 element does not require expression of functions necessary for **stable maintenance** or transfer of extrachromosomal forms of SLP1.

L23 ANSWER 2 OF 5 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 88274753 MEDLINE
DOCUMENT NUMBER: 88274753 PubMed ID: 3453403
TITLE: Development of a plasmid-cloning system for **Streptomyces** viridochromogenes Tu494.
AUTHOR: Strauch E; Wohlleben W; Puhler A
CORPORATE SOURCE: Lehrstuhl fur Genetik, Fakultat fur Biologie, Universitat Bielefeld, FRG.
SOURCE: JOURNAL OF BASIC MICROBIOLOGY, (1987) 27 (8) 449-55.
Journal code: 8503885. ISSN: 0233-111X.
PUB. COUNTRY: GERMANY, EAST: German Democratic Republic
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198808
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880818

AB A plasmid-cloning system was developed for **Streptomyces** viridochromogenes Tu494, a producer of the tripeptide antibiotic phosphinothricyl-alanyl-alanine (PTT). Parameters affecting protoplast formation and transformability of S. viridochromogenes were investigated in detail. A procedure giving rise to transformation efficiencies of 10(4)-10(5) transformants per microgram DNA was worked out. Several **Streptomyces** plasmid vectors such as pIJ350, pIJ61, pEB2, pGM4 and pSW2 were tested in S. viridochromogenes. Some of these vectors (pGM4, pEB2) showed a high copy number, whereas the copy number of others (pIJ350, pIJ61 and pSW2) was markedly lower. Under non-selective conditions some of the vectors (pIJ350, pEB2) were not stably maintained, in contrast to the vectors pGM4 and pSW2 which did not require any selection pressure for **stable maintenance**. Therefore,

the plasmid vectors pGM4 and pSW2 derived from endogenous replicons of **Streptomyces** ghanaensis strains represent appropriate plasmid vehicles for cloning experiments in S. viridochromogenes.

L23 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 87085426 MEDLINE
DOCUMENT NUMBER: 87085426 PubMed ID: 3025335
TITLE: Properties of in vitro recombinant derivatives of pJV1, a multi-copy plasmid from **Streptomyces** phaeochromogenes.
AUTHOR: Bailey C R; Bruton C J; Butler M J; Chater K F; Harris J E; Hopwood D A
SOURCE: JOURNAL OF GENERAL MICROBIOLOGY, (1986 Aug) 132 (Pt 8) 2071-8.
Journal code: 0375371. ISSN: 0022-1287.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198702
ENTRY DATE: Entered STN: 19900302
Last Updated on STN: 19900302
Entered Medline: 19870219

AB The 10.8 kb plasmid pJV1, isolated from **Streptomyces** phaeochromogenes, has a high copy number (about 150) and a broad host range among **Streptomyces** spp. Several pJV1 derivatives carrying the thiostrepton resistance gene (tsr) of S. azureus were made. One derivative, pWOR191, was shown to promote its own transfer and to mobilize chromosomal markers in S. lividans. Another derivative, pWOR109, was non-transmissible. Deletion in vitro of a segment of pWOR109 gave pWOR120 (5.6 kb), which has single BamHI and Bg/II sites shown to be capable of accepting 'foreign' DNA such as a previously cloned S. antibioticus DNA fragment encoding tyrosinase, giving vectors (pWOR125, pWOR126) with properties resembling the well-established multicopy vector pIJ702. Shuttle vectors capable of functioning in both S. lividans and Escherichia coli were also constructed. The region of pJV1 essential for replication and maintenance was localized to a 2.5 kb segment. **Stable maintenance** of pWOR109 and pWOR120 was observed in the presence of derivatives of pIJ101, the progenitor of pIJ702.

L23 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1982:222682 BIOSIS
DOCUMENT NUMBER: PREV198273082666; BA73:82666
TITLE: GENETIC STUDIES OF THE FERTILITY PLASMID SCP-2 AND ITS SCP-2 VARIANTS IN **STREPTOMYCES**-COELICOLOR A-32.
AUTHOR(S): BIBB M J [Reprint author]; HOPWOOD D A
CORPORATE SOURCE: DEP GENET, STANFORD UNIV SCH MED, STANFORD UNIV MED CENT, STANFORD, CALIF 94305, USA
SOURCE: Journal of General Microbiology, (1981) Vol. 126, No. 2, pp. 427-442.
CODEN: JGMIAN. ISSN: 0022-1287.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The plasmid SCP2, initially discovered through the occurrence of a high fertility variant, SCP2*, is a self-transmissible fertility factor capable of promoting chromosomal recombination within S. coelicolor A3(2). Further high fertility variants of SCP2, similar to SCP2*, were isolated from among recombinants produced in matings involving SCP2, and their genetic properties were compared. SCP2 and its derivatives elicit lethal zygosis on transfer into an SCP2- recipient; this plasmid-determined phenotype allowed the isolation of SCP2- strains and the detection of the interspecific transfer of SCP2* by mating from S. coelicolor to S.

parvulus and S. lividans, whereupon it underwent **stable maintenance**. The transfer genes of SCP2 and SCP2*, which are not normally fully expressed, were shown to undergo transient derepression on entry into an SCP2- strain. An entry disadvantage system determined by SCP2 and SCP2* was recognized.

L23 ANSWER 5 OF 5 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 80220553 MEDLINE
DOCUMENT NUMBER: 80220553 PubMed ID: 6770876
TITLE: [Plasmids as cloning vehicles (author's transl)]. Plasmide als Kloniervehikel.
AUTHOR: Goebel W
SOURCE: ARZNEIMITTEL-FORSCHUNG, (1980) 30 (3a) 533-40. Ref: 28
Journal code: 0372660. ISSN: 0004-4172.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198008
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800825

AB Plasmids are regulated autonomously replicating DNA elements, which have been used successfully for the in vitro insertion and the transfer and **stable maintenance** of defined foreign DNA fragments into bacteria and lower eukaryontes. For Escherichia coli a large set of ColE1 derivatives have been developed and have been used for cloning of DNA fragments from many biological systems. More recently plasmids have been also isolated and modified for the use as cloning vehicle for other bacteria like Bacillus subtilis, Pseudomonas and **Streptomyces** and for the yeast Saccharomyces cerevisiae.

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